PYRETHRUM

Antonia Glynne-Jones of the Gooddeed Chemical Company in Aylesbury, UK, describes a unique biopesticide

Historical introduction

The white Chrysanthemum flower, pyrethrum, is mentioned in early Chinese history and it is believed to have passed into Europe along the silk routes. However, the species of the plant was unknown, so for convenience the history of pyrethrum usually starts with the mention in 1847 of the identified species *Chrysanthemum cinerariaefolium* found growing in Dalmatia (now part of Croatia). Later, ground pyrethrum flowers could be found for sale in most European pharmacies as 'Dalmatian Insect Powder'. From 1885, bales of dried flowers were exported to the USA and, during 1913, 500 tonnes were shipped. The outbreak of World War I ended these exports and the USA started importing dried flowers from Japan, which had started growing the crop in 1886. The primary uses for the ground flowers were for the control of body lice on humans and animals, and crawling insects in the home.

In 1917, the US Navy made the first pyrethrum extracts by percolating ground flowers with kerosene, which were then incorporated into space sprays for use against houseflies and mosquitoes. Pyrethrum products became available for general use even though the chemistry of the active ingredient(s) in pyrethrum was unknown. In 1924, when Staudinger and Ruzicka, working in Switzerland, published a series of classical papers on the chemistry of pyrethrum which showed that the insecticidal properties were due to the presence of two esters which they named Pyrethrin I and Pyrethrin II.

This work permitted other chemists to develop analytical methods and these were used by F. Tattersfield at Rothamsted Experimental Station at Harpenden, UK, to undertake a fundamental study "Pyrethrum Flowers – A Quantitative Study of their Development". The combination of identification of the active ingredients, followed by their chemical assay linked with a study of the development of the active principles in the flowers (Tattersfield, 1931) set pyrethrum on a technically orientated path where it has prospered as a unique botanical biopesticide, differing from many others whose active molecules could not be easily analyzed.

Production

The pyrethrum plant (Figure 1) is of temperate origin and requires an exposure to a cold period of less than 10°C to initiate flowering. Commercial production is divided between temperate climates, *e.g.* Tasmania (the most southerly state of Australia), Norfolk in England and elevated areas above 2000 m near the Equator, *e.g.* Kenya and Ecuador. Yields of dried flowers may be highest under temperate conditions, but one intense flowering period presents acute harvesting and drying problems, when every attempt has to be made to pick the flowers when the yield of pyrethrins in the flower is at its optimum. In contrast, in places like Kenya, the day length and average temperatures show little variation extending flowering and subsequent harvesting to a period of several months (bud initiation happens during cold nights). Furthermore, the regular extended deliveries of dried flowers to the processing plant reduces costs.

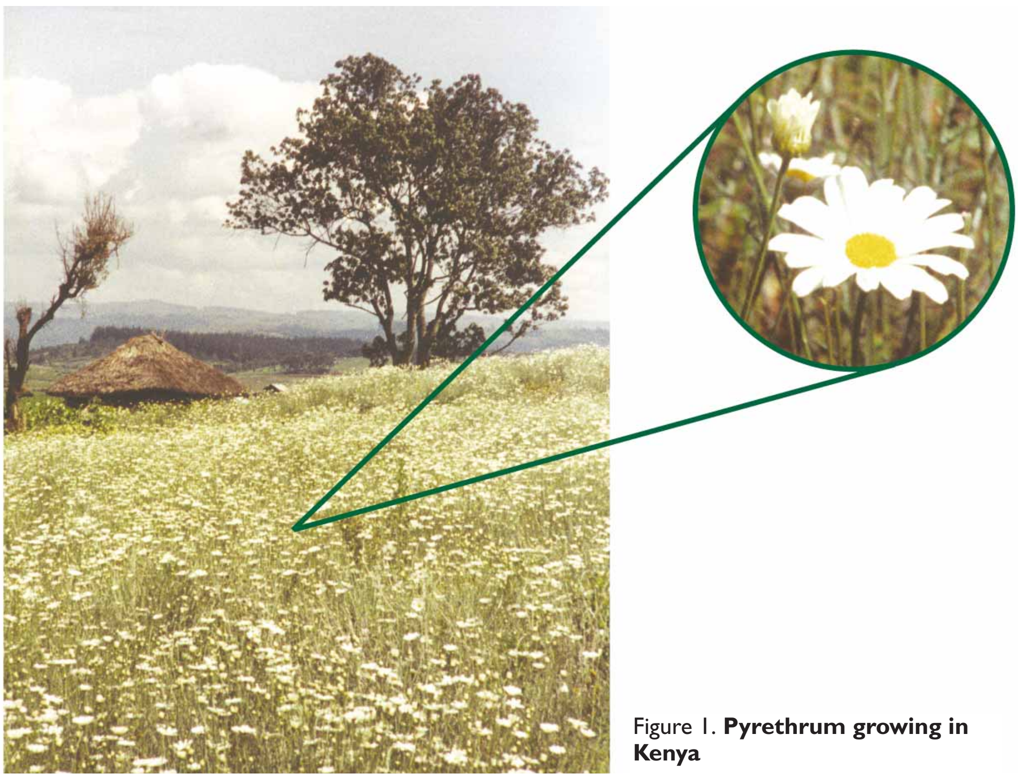

Figure 1. **Pyrethrum growing in Kenya**

The annual world production of dried flowers has rarely exceeded 20,000 metric tonnes and, with an average pyrethrins content of 1.5%, the potential yield is 30 kg of 50% extract per tonne. However, with losses at various processing stages the actual yield is nearer 25 kg, giving a potential annual world production of 500 tonnes of 50% pale extract. Annual sales at consumer level, estimated using confidential data from the largest formulators, indicate a figure of $300 million. Industrial usage related to food processing is probably approximately another $100 million, and minor uses are probably in the region of $20 million.

In the past 40 years, there have been long periods when pyrethrum extract has been in short supply – as it is at present – then shorter periods in surplus. The current shortage means that most usage of pyrethrum is in the USA, as producers have tended to give that country preference with their limited supplies. This roller-coaster availability has encouraged the development and use of synthetic alternatives, especially outside the USA, but none of these alternatives have all the unique properties of natural pyrethrum.

Composition and formulation

Today, pyrethrum is traded in two forms:

- a powder containing the flowers ground to a standard mesh size and stabilized against degradation with butylated hydroxy toluene (BHT) as an antioxidant.
- a refined concentrated extract also stabilized with BHT containing 50% or 25% pyrethrins.

The refining process may use solvents such as hexane and methyl alcohol or supercritical carbon dioxide, the latter process having the advantage of avoiding any heating of the pyrethrins during extraction. During processing great care has to be taken to protect the esters from degradation due to oxidation; free radicals need to be eliminated and the processing temperatures kept below 60°C. The refining process removes impurities that can cause allergenic reactions on human skin and also various waxes and resins that might block aerosol valves.

The six esters comprising the active ingredients are listed in Figure 2 and, whilst the relative amounts of each vary depending on the particular plant type, geographical source and time of harvest, the average assay would be as given in Table 1.

Table 1. Relative proportions of the six esters in a typical 50% extract of pyrethrum.

cinerin I	3.7%		
jasmolin I	2.0%	pyrethrins I 24.7%	
pyrethrin I	19.0%		
			total pyrethrins 50%
cinerin II	5.8%		
jasmolin II	2.0%	pyrethrins II 25.3%	
pyrethrin II	17.5%		

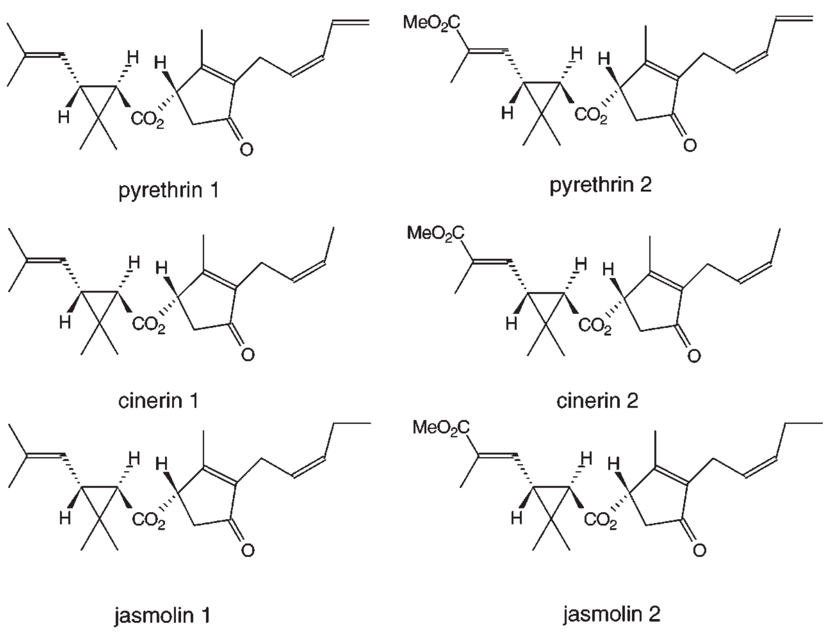

Figure 2. **Structural formulae of pyrethrins**
Note: pyrethrin I, cinerin I and jasmolin I are referred collectively as **Pyrethrins I,** while pyrethin II, cinerin II and jasmolin II are referred to as **Pyrethrins II**. (Crombie, 1995).

Extensive biological tests have shown that whilst extract from different sources and batches may vary slightly in insecticide potency, such differences disappear when pyrethrum is used with piperonyl butoxide (PBO) as a synergist. Today, the majority of pyrethrum formulations are synergised by the addition of piperonyl butoxide (Glynne Jones, 1999); this makes them more cost-effective and since this biopesticide is relatively expensive and often in short supply, this is a very important consideration. The ratio of PBO to pure pyrethrins averages at 4:1 – the final choice being influenced by the cost of the pyrethrum extract.

Efficacy as an insecticide

The main use of pyrethrum at present is in household formulations to kill houseflies, cockroaches and mosquitoes (Figure 3). Insects react very quickly when dosed with pyrethrum, and this quick knock-down effect is a very valuable property for household insecticides as the user sees the onset of paralysis within 2–3 minutes. Pyrethrum acts on a very wide spectrum of insect species – more so than with most individual synthetic insecticides. It is also a very powerful repellent to mosquitoes, and micro doses – *e.g.* as found in the smoke from mosquito coils – have the unique effect of preventing a hungry female mosquito from biting. The process of piercing the skin using saliva injected as a lubricant, finding and piercing a blood capillary followed by sucking of blood into the insect is a very precise and complicated process and co-ordination is lost when even a few molecules of pyrethrum are present.

Synergised pyrethrum formulations are particularly effective against the mosquitoes and midges, which bite humans, and to date there have been no reports of resistance developing in these species to this biopesticide. Pyrethrins are very quickly degraded in sunlight leaving no toxic residues and are ideal for use as pre-harvest sprays to remove insect pests on edible crops – up to 24 hours before harvest.

Safety to man and animals

For the first 130 years of usage, on or near humans, the only safety complaints were due to the appearance of skin allergies. The most vocal complaints were from the British and Allied soldiers in World War II who used pyrethrum ointments based on crude oleoresin extracts to repel mosquitoes whilst fighting in tropical areas. These negative comments led to the refining of the crude extracts. At the same time, the first Freon-based aerosols were being developed which required refined extracts–now described as pale extracts as they are dewaxed and decolourised.

During the next 40 years, pyrethrum was considered as being a very safe product for use on or near humans and animals. From 1930–1955 pyrethrum extract was the anthelminthic of choice for young children in France, and from 1950 it was added in an alcoholic solution to potable water as a simple but effective control of the small water crab *Ascellus aquaticus* found in water mains in Europe. A very low dose of pyrethrum caused these crabs, which blocked the filters, to lose their grip and then they could be washed away. In Australia from 1963 onwards, many millions of cans of liquid repellents containing up to 0.5% w/w of pyrethrins were applied to human skin without any significant adverse effects being reported. In the USA, up to 1973 household products containing synergised pyrethrum could be labeled as "nontoxic to human and pets" and there has been continuous use of pyrethrum-based formulations to control head lice in children in the Western world since refined extracts became available.

In 1999 the EPA in the USA having examined data from the long-term feeding of extremely large doses of pyrethrum extract to rodents suggested it was "likely to be a human carcinogen by the oral route". In practice the oral daily dosing of up to 5000 ppm during one's lifetime would never take place.

The WHO/FAO Joint Meeting on Pesticide Residues (JMPR) have issued a report on the safety of pyrethrum extract following their recent review (Solecki, 1999). They take a more pragmatic view and because of its importance this is quoted in full:

> *"In a two-year study of toxicity and carcinogenicity in rats and an 18-month study of carcinogenicity in mice, the NOAEL [no observed adverse effect level] was 100 ppm in both species, equal to 14 and 4 mg kg^{-1} body weight per day in mice and rats, respectively. The liver was the main target. A treatment-related effect on the incidence of lung tumours was seen in mice and increased incidences of benign tumours of the skin, liver, and thyroid were observed in rats. The increased incidences of hepatocellular adenomas were associated with persistent induction of cytochrome P450 enzymes and hepatocellular hypertrophy, suggesting that pyrethrins are rodent-specific hepatoproliferative carcinogens. Enzyme induction leading to increased clearance of thyroid hormones would also be consistent with the higher incidence of follicular hyperplasia and follicular adenomas. However, additional studies on the mechanism of formation of the liver and thyroid tumours are required. The Meeting concluded that the increased tumour incidences caused by pyrethrins are threshold phenomena of negligible relevance to the low doses to which humans are exposed."*

The future for pyrethrum

There is a general agreement that if regular supplies of high quality pyrethrum extract were available at stable price levels, the present market would expand in many areas. The three most important would probably be:

- in mosquito control in both the home and for mosquito abatement projects on or near urban areas where safety to humans and no residues are prime considerations.
- in home and garden formulations and increased use in specialised horticulture, following restrictions placed on organophosphate insecticides.

Pyrethrum Post 1948–99 on CD-ROM

Available from "Friends of Pyrethrum", 9 Cole Road, Aylesbury, Bucks, HP21 8SU UK. Tel: +44 (0)1296 392408 Fax: +44 (0)1296 392404 and a single copy costs $150 / £100.

The scientific journal, *Pyrethrum Post*, sponsored and financed by the Kenya pyrethrum industry, has been published in 20 volumes at regular intervals since 1948 and contains a wealth of technical and practical information on the chemistry and use of this biopesticide. For years the unavailability of editions of the journal has been a constant irritation to users, and researchers of natural pyrethrum. Many early editions have long been out of print and newer editions have been sporadically available. Now, this has disappeared thanks to a new CD-ROM *Pyrethrum Post* which contains all volumes of the journal from 1948 to 1999.

One easily navigates the CD-ROM in the same way as with a digitized encyclopedia – by keywords and subjects. Text and diagrams are excellent. The photographs accompanying the articles are rather disappointing in quality but still acceptable.

Most of the important papers on pyrethrum are included on this CD-ROM, from the agronomics of cultivation and propagation to the uses and structural niceties of the individual insecticidal pyrethrin analogs. One can read about the use of pyrethrum to disinfect water mains to its use in public health and industrial applications. There are reviews of the methods of refining pyrethrum extract as well as evaluations of various synergists and their development.

Review by D. MacIver, Fairfield American Corp.

Figure 3. **Label for a pyrethrum product formulated as a mosquito repellent.**

- in organic farming as it continues to expand. Pyrethrum is already included in most lists of approved organic insecticides throughout the world and supported by an extensive package of toxicological studies, will inevitably become the dominant insecticide. A rapid expansion of organic farming has happened during the past 5 years but, because of an acute shortage, only small amounts of pyrethrum at very high prices have been available for purchase outside the USA.

Kenya once produced and sold 14,400 tonnes of dried flowers as extract and powder in one year (1971/72) and could expand back to this level. Tasmania with advanced modern technology such as plant tissue culture and refining with supercritical carbon dioxide could double sales once their present extraction facilities are expanded and the area planted to pyrethrum is increased. Smaller producers in Tanzania and France would prosper under stable marketing conditions.

The formation of an association of pyrethrum growers, with the main purpose of setting up and financing a stockpile of extract would be greatly welcomed by formulators. Already the majority of producers have joined together to finance toxicity studies, an essential requirement for survival today, so expanding this association to organise a stockpile would not be difficult.

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Further Reading

"Pyrethrum, the natural insecticide" edited by John E. Casida, published by Academic Press (1973)
"Pyrethrum Flowers–Production, Chemistry, Toxicology, and Uses". Ed. John E. Casida and Gary B. Quistad. Oxford University Press (1995)

Antonia Glynne-Jones was born in Kenya at Nakuru, a small town in the Rift Valley, which housed the pyrethrum processing plants and the laboratories and administrative offices of the Pyrethrum Board of Kenya. Following her higher education in the UK at Lowther College in North Wales and Bristol University, she returned to Africa to work in the pharmaceutical industry and 6 years later went back to England to run a small speciality chemical company, Goodeed Chemicals, the UK subsidiary of Endura Spa of Bologna, Italy, the world's largest manufacturer of the synergist piperonyl butoxide. Pyrethrum was soon added to Goodeed's list of speciality chemicals and today with Antonia as Managing Director, Goodeed is proud to claim to be the largest supplier of pyrethrum in the UK.

IN THE NEXT ISSUE

It is hoped that the next issue of *Pesticide Outlook* will include articles on such diverse topics as the maize genome, pesticides from lichens, minor uses of pesticides, insect pests of palms, FAO Specifications for Pesticides and methyl bromide alternatives.